

In the Claims

Please amend the claims as follows:

1.-42 (Canceled)

43. (Currently Amended) A ~~non-naturally occurring protein~~ polypeptide which inhibits human neutrophil elastase, and which ~~is a protein comprising~~ comprises at least the core sequence of a non-naturally occurring Kunitz domain, said Kunitz domain being more similar in sequence to comprising at least two modifications of the core amino acid sequence 3-57 of ITI-D2 of the carboxyl-proximal Kunitz domain of the human Inter- α -Trypsin-Inhibitor (ITI-D2) set forth in SEQ ID NO:25 ~~than to the core sequence 5-55 of BPTI when its cysteines are aligned with those of BPTI and ITI-D2, but said domain differing from ITI-D2 wherein the~~ modifications are in that at least one of the following conditions applies amino acid substitutions selected from the group of substitutions consisting of:

- (a) a substitution of the residue corresponding to ITI-D2 residue 3 is position 3 of SEQ ID NO:25 with Glu,
- (b) a substitution of the residue corresponding to ITI-D2 residue 15 is position 15 of SEQ ID NO:25 with Ile,
- (c) a substitution of the residue corresponding to ITI-D2 residue 18 is position 18 of SEQ ID NO:25 with Phe,
- (d) a substitution of the residue corresponding to ITI-D2 residue 19 is position 19 of SEQ ID NO:25 with Pro, or and
- (e) a substitution of the residue corresponding to ITI-D2 residue 20 is position 20 of SEQ ID NO:25 with Arg.

44. (Currently Amended) The ~~protein~~ polypeptide of claim 43, ~~wherein conditions which~~ comprises the amino acid substitutions stated in each of clauses (b) through (d) apply.

45. (Currently Amended) The ~~protein~~ polypeptide of claim 43, wherein the ~~core~~ polypeptide comprises the amino acid sequence is set forth in SEQ ID NO:27 EpiHNE4 (Epi-HNE-4).

46. (Currently Amended) The ~~protein~~ polypeptide of claim 43, wherein the ~~core~~ polypeptide comprises the amino acid sequence is set forth in SEQ ID NO:26 EpiHNE3 (Epi-HNE-3).

47. (Currently Amended) The ~~protein~~ polypeptide of claim 43 which has an affinity for human neutrophil elastase HNE such that its K_D is less than 5 pM.

48. (Currently Amended) The ~~protein~~ polypeptide of claim 43 which has an affinity for human neutrophil elastase HNE such that its K_D is less than 7 pM.

49. (New) A method of inhibiting human neutrophil elastase which comprises contacting human neutrophil elastase with an inhibitory effective amount of a polypeptide of any one of claims 43-48.

50. (New) A method of inhibiting harmful human neutrophil elastase activity in a subject which comprises administering to the subject an inhibitory effective amount of polypeptide of any one of claims 43-48.

51. (New) A method of treating emphysema in a subject which comprises administering to the subject a therapeutically effective amount of a polypeptide of claims 43-48.

52. (New) A method of treating cystic fibrosis in a subject which comprises administering to the subject a therapeutically effective amount of a polypeptide of claims 43-48.